

**Amendments to the Claims:**

**Listing of Claims:**

Claim 1 (currently amended): ~~Use of inhibitors of the expressed proteins, or peptides derived therefrom, of TCF target genes whose expression is regulated by TCF/β-catenin complexes for the preparation of a therapeutical composition for the treatment of cancers in which TCF/β-catenin signalling is deregulated~~ A method for treating a patient with cancer in which TCF/β catenin signalling is deregulated comprising administering a therapeutic composition to said patient comprising an inhibitor of the expressed protein, or peptide derived therefrom, of a TCF target gene whose expression is regulated by a TCF/β catenin complex.

Claim 2 (currently amended): ~~Use as claimed in The method of claim 1, wherein the inhibitors are antibodies or derivatives~~ inhibitor is an antibody or derivative thereof directed against the expression product ~~products of the target gene genes that are~~ is expressed on the cell membrane.

Claim 3 (currently amended): ~~Use as claimed in The method of claim 1 or 2, wherein the antibodies or derivatives~~ antibody or derivative thereof are is directed against a peptide, which is chosen from the group consisting of:

H-YEKELSEYNATALKSPC-NH<sub>2</sub>; H-PFSPQFASVNC-NH<sub>2</sub>;  
H-PGSYKAKQGEGPC-NH<sub>2</sub>; H-CQMNSVQLDGLPDARY-OH;  
H-CGYDARQKPEVDQQ-OH; H-CKGVLSNISSITLGGFD-OH; H-HSALEDVEALHPRKER-C-NH<sub>2</sub>;  
and H-CNYHSHAGAREHRRGD-OH.

Claim 4 (currently amended): ~~Use as claimed in claim 1, 2 or 3~~ The method of claim 3, wherein the derivatives are derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, and other antibody-derived molecules.

Claim 5 (currently amended): ~~Use as claimed in claim 1~~ The method of claim 1, wherein the inhibitors are small molecules inhibitor is a small molecule that interferes interfering with the biological activity of the protein expressed by the target gene.

Claim 6 (currently amended): ~~Use of inhibitors of the mRNA transcripts of TCF target genes whose expression is regulated by TCF/β catenin complexes for the preparation of a therapeutical composition for the treatment of cancers in which TCF/β catenin signalling is deregulated. A method for treating a patient with cancer in which TCF/β catenin signalling is deregulated comprising administering a therapeutic composition to said patient comprising an inhibitor of the mRNA transcript of a TCF target gene whose expression is regulated by a TCF/β catenin complex.~~

Claim 7 (currently amended): ~~Use as claimed in claim 6~~ The method of claim 6, wherein the inhibitors are is an antisense molecule, molecules, in particular antisense RNA or antisense oligodeoxynucleotides.

Claim 8 (currently amended): ~~Use as claimed in claim 6~~ The method of claim 6, wherein the inhibitors are inhibitor is a double stranded RNA molecules for RNA interference.

Claim 9 (currently amended): ~~Use as claimed in claim 1~~ The method of claim 6, wherein the treatment comprises gene therapy.

Claim 10 (currently amended): ~~Use as claimed in any one of the claims 1-9~~ The method of claim 1 or 6, wherein the therapeutic therapeutical composition is for treatment of Familial Adenomatous Polyposis (FAP).

Claim 11 (currently amended): ~~Use as claimed in any one of the claims 1-9~~ The method of claim 1 or 6, wherein the therapeutic therapeutical composition is for treatment of colorectal cancer.

Claim 12 (currently amended): ~~Use as claimed in any one of the claims 1-9~~ The method of claim 1 or 6, wherein the therapeutic therapeutical composition is for treatment of melanomas.

Claim 13 (cancelled)

Claim 14 (currently amended): ~~Use as claimed in claim 13, wherein the diagnosis is performed by means of histological analysis of a tissue specimens using specific antibodies directed against target gene products, and/or in situ hybridization analysis of TCF/β catenin target gene expression levels in tissue specimens using specific RNA probes directed against TCF/β catenin target gene sequences~~ A method for diagnosing a patient with cancer in which TCF/β catenin

signaling is deregulated wherein the diagnosis is by histological analysis of a tissue specimen using (i) a specific antibody directed against a target gene product, and/or (i) *in situ* hybridization analysis of a TCF/β-catenin target gene expression levels in tissue specimens using specific RNA probes directed against the TCF/β-catenin target gene sequence.

Claim 15 (currently amended): Use as claimed in any one of the claims 1-14. The method of claim 1, 6 or 14, wherein the target gene is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

Claim 16 (currently amended): Use as claimed in any one of the claims 1-15. The method of claim 1, 6 or 14, wherein the target gene is CD44, comprising a cDNA sequence, which is at least 90% homologous to the cDNA sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18 or Figure 19.

Claim 17 (currently amended): Use as claimed in any one of the claims 1-15. The method of claim 1, 6 or 14, wherein the target gene is GPR49, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

Claim 18 (currently amended): Use as claimed in any one of the claims 1-15. The method of claim 1, 6 or 14, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21 (SEQ. ID. No 5).

Claim 19 (currently amended): Use as claimed in any one of the claims 1-15. The method of claim 1, 6 or 14, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 22 (SEQ. ID. No 7).

Claim 20 (currently amended): ~~Use as claimed in any one of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 23 (SEQ. ID. No 9).

Claim 21 (currently amended): ~~Use as claimed in any one of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

Claim 22 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences as shown in Figure 17 or 18.

Claim 23 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

Claim 24 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

Claim 25 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

Claim 26 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

Claim 27 (currently amended): ~~Use as claimed in any of the claims 1-15~~ The method of claim 1, 6 or 14, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 24 (SEQ ID No. 12).

Claim 28 (currently amended): Inhibitor compound directed against the expressed proteins, or peptides derived therefrom, of a TCF target gene the expression of which is regulated by a TCF/β-catenin complexes ~~for use in the treatment of colorectal cancer~~.

Claim 29 (currently amended): The inhibitor inhibitor compound as claimed in of claim 28, which wherein said inhibitor compound is an antibody or derivative derivatives thereof directed against the expression products of a target gene that is expressed on ~~the a~~ cell membrane.

Claim 30 (currently amended): The inhibitor inhibitor compound as claimed in of claim 29 wherein the antibodies or derivatives thereof are directed against a peptide, which is chosen from the group consisting of:

H-YEKELSEYNATALKSPC-NH2; H-PFSPQFASVNC-NH2;  
H-PGSYKAKQGEGPC-NH2; H-CQMNSVQLDGLPDARY-OH;  
H-CGYDARQKPEVDQQ-OH; H-CKGVLSNISSITLGGFD-OH; H-HSALEDVEALHPRKER-C-NH2;  
and H-CNYHSHAGAREHRRGD-OH.

Claim 31 (currently amended): The inhibitor inhibitor compound as claimed in of claim 29 or 30, wherein the derivative is selected from the group consisting of scFv fragments, Fab fragments, chimeric antibodies, bifunctional antibodies, or other antibody-derived molecules.

Claim 32 (currently amended): The inhibitor inhibitor compound as claimed in of claim 28, which wherein said inhibitor compound is a small molecule that interferes interfering with the biological activity of the protein expressed by the target gene.

Claim 33 (currently amended): The inhibitor inhibitor compound directed against the transcription product (mRNA) of a TCF target gene the expression of which is regulated by TCF/β-catenin complexes for use in the treatment of colorectal cancer.

Claim 34 (currently amended): The inhibitor inhibitor compound as claimed in of claim 33, which wherein said inhibitor compound is an antisense molecule, in particular that is an antisense RNA or an antisense oligodeoxynucleotide.

Claim 35 (currently amended): The inhibitor inhibitor compound as claimed in of claim 34, which wherein said inhibitor compound is a double stranded RNA molecule for RNA interference.

Claim 36 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claims 28 or 33~~, wherein the target gene is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family 7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.

Claim 37 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claim 28 or 33~~, wherein the target gene is CD44, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 17 (SEQ. ID. No 1), Figure 18, or Figure 19.

Claim 38 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claim 28 or 33~~, wherein the target gene is GPR49, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 20 (SEQ. ID. No 3).

Claim 39 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claim 28 or 33~~, wherein the target gene is EPBH4, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 21(SEQ. ID. No 5).

Claim 40 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claim 28 or 33~~, wherein the target gene is GPX2, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 22 (SEQ. ID. No 7).

Claim 41 (currently amended): ~~The inhibitor~~ compound as claimed in any one of the claims 28-35 ~~of claim 28 or 33~~, wherein the target gene is RGMR, comprising a cDNA sequence which is at least 90% homologous to the sequence shown in Figure 23 (SEQ. ID. No 9).

Claim 42 (currently amended): The inhibitor compound Inhibitor compound as claimed in any one of the claims 28-35 of claim 28 or 33, wherein the target gene is Tspan5, represented by a sequence which is at least 90% homologous to the sequence shown in Figure 24 (SEQ. ID. No 11).

Claim 43 (currently amended): The inhibitor compound as claimed in any of the claims 28-35 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 17 or 18.

Claim 44 (currently amended): The inhibitor compound as claimed in any of the claims 28-35 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 20 (SEQ ID No. 4).

Claim 45 (currently amended): The inhibitor compound as claimed in any of the claims 28-35 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 21 (SEQ ID No. 6).

Claim 46 (currently amended): The inhibitor compound as claimed in any of the claims 28-35 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 22 (SEQ ID No. 8).

Claim 47 (currently amended): The inhibitor compound as claimed in any of the claims 28-35 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 23 (SEQ ID No. 10).

Claim 48 (currently amended): The inhibitor compound as claimed in any of the claims 1-15 of claim 28 or 33, wherein the expressed protein comprises a sequence which is at least 90% homologous to the protein sequences of Figure 24 (SEQ ID No. 12).

Claim 49 (original): Diagnostic agent for diagnosing cancers in which TCF/β-catenin signaling is deregulated.

Claim 50 (currently amended): The diagnostic Diagnostic agent as claimed in of claim 49, which is a specific antibody directed against the expressed protein of a TCF/β-catenin target gene or an RNA probe specific for a TCF/β-catenin target gene sequence.

Claim 51 (currently amended): Therapeutical composition for the treatment of cancer cancers in which the TCF/β-catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more of the inhibitor compounds as claimed in claims 28-48 of claims 28 and 33.

Claim 52 (currently amended): Diagnostic composition for the diagnosis of cancer cancers in which the TCF/β-catenin signaling is deregulated, comprising a suitable excipient, carrier and/or diluent and one or more diagnostic compounds as claimed in claim 49 or 50.

Claim 53 (currently amended): The compositions Compositions as claimed in of claim 51 or 52, wherein the cancer is colorectal cancer, melanoma or Familial Adenomatous Polyposis (FAP).

Claim 54 (currently amended): Method for the development of therapeutic inhibitor compounds as claimed in claims 28-48 claim 28 or 33, which method comprises the steps:

- a) identification of genes regulated by TCF/β-catenin in colon carcinoma cells, in particular by using microarray technologies;
- b) validation of one or more of the identified genes as potential target gene(s) for the therapeutic compound by one or more of the following methods:
  - confirmation of the identified gene by Northern Blot analysis in colon carcinoma cell-lines;
  - determination of the expression profile of the identified gene in human colorectal tumors and normal tissue;
  - determination of the functional importance of the identified target genes for colorectal cancer;
- c) production of the expression product of the target gene; and
- d) use of the expression product of the target gene for the production or design of a therapeutic compound.

Claim 55 (currently amended): The method Method as claimed in of claim 54, wherein the target gene identified in step a) is selected from the group consisting of CD44, KIT, G protein-coupled receptor 49 (GPR49), Solute Carrier Family 12 member 2 (SLC12A2), Solute Carrier Family

7 member 5, Claudin 1(CLDN1), SSTK serine threonine kinase, FYN oncogene, EPHB2 receptor tyrosine kinase, EPHB3 receptor tyrosine kinase, EPHB4 receptor tyrosine kinase, ETS2, c-Myc, MYB, ID3, POLE3, Bone Morphogenetic Protein 4 (BMP4), Kit ligand (KITLG), GPX2, GNG2, CDCA7, ENC1, the gene identified with Celera ID hCG40185, the gene identified with Celera ID hCG1645335, the gene represented by IMAGE clone 1871074, the gene identified with Celera ID hCG27486, the gene represented by IMAGE clone 294873, the gene represented by IMAGE clone 940994, the gene identified with Celera ID 39573, the gene represented by IMAGE clone 753028, the gene identified with Celera ID hCG37727, the gene identified with Celera ID hCG40978, and the gene identified with Celera ID hCG1811066.